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A novel 2*H*-azirin-3-amine as a synthon for a sulfur-containing dipeptide segment

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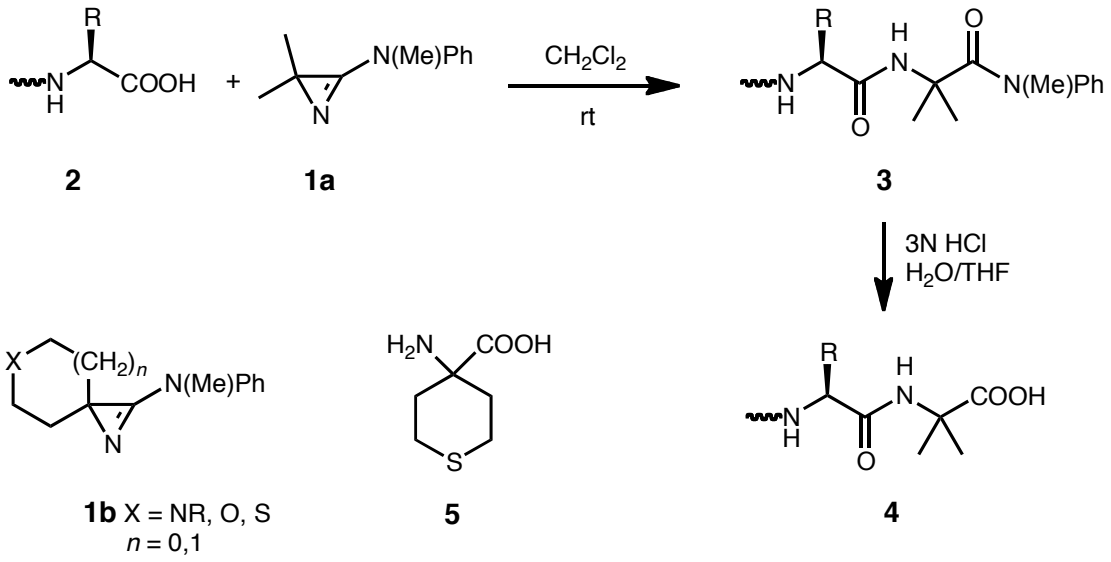
Starting with tetrahydro-2*H*-thiopyran-4-carboxylic acid and methyl prolinate, the novel 2*H*-azirin-3-amine (*S*)-*N*-(1-aza-6-thiaspiro[2.5]oct-1-en-2-yl)proline methyl ester was synthesized. In reactions with benzoic acid, thiobenzoic acid, and Boc-valine, respectively, its usefulness as a synthon for the dipeptide (*S*)-*N*-[(4-aminotetrahydro-2*H*-thiopyran-4-yl)carbonyl]proline in peptide synthesis was demonstrated.

Keywords: 2*H*-azirin-3-amines; *N*-(1-aza-6-thiaspiro[2.5]oct-1-en-2-yl)proline methyl ester; α-amino acids; 4-aminotetrahydro-2*H*-thiopyran-4-carboxylic acid; sulfur-heterocyclic amino acids

1. Introduction

In the past we have shown that 2,2-disubstituted 2*H*-azirin-3-amines **1** are building blocks for 2,2-disubstituted α-amino acids in the synthesis of heterocycles as well as of peptides [1–3]. The smooth coupling reaction with *N*-protected amino acids or peptides **2** to give extended peptide amides **3** does not need any additional reagent, and the subsequent hydrolysis of the terminal amide group leading to peptides **4** occurs selectively (Scheme 1). This method has been used successfully towards the synthesis of natural peptaibol antibiotics [4–10].



Scheme 1. Reaction of 2*H*-azirin-3-amines with amino acids and selective hydrolysis; the 'azirine/oxazolone method'

Spiroheterocyclic 2*H*-azirines of type **1b**, which serve as synthons for heterocyclic α-amino carboxylic acids, form a special class of these synthons [11–15]. For example, the tetrahydro-2*H*-thiopyran derivative **1b** (X = S, n = 1) has been used to prepare tripeptides containing 4-aminotetrahydro-2*H*-thiopyran-4-carboxylic acid (**5**) [12]. This heterocyclic amino acid has been described as a cyclic homocysteine [16]

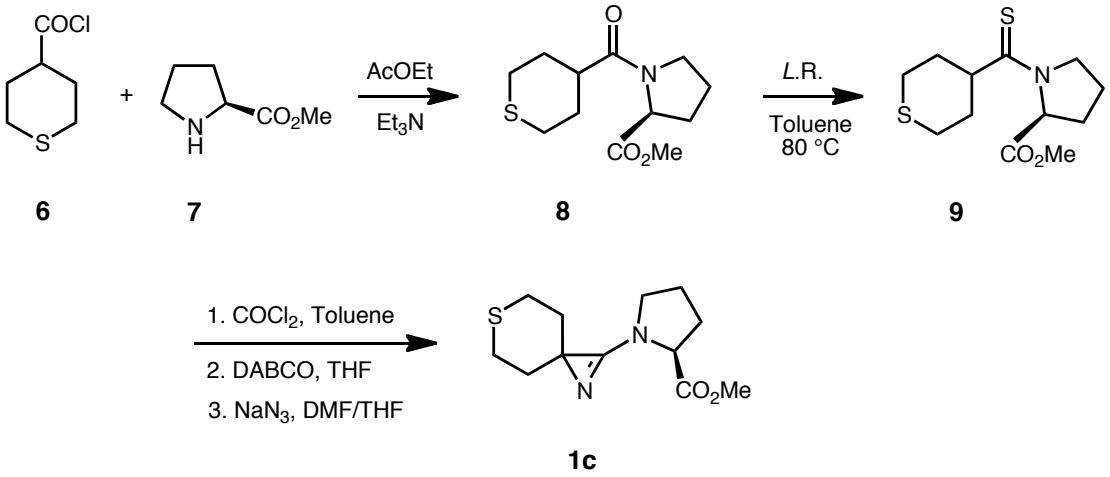
or methionine analog [17], and was prepared via Strecker synthesis [18], the Bucherer-Bergs reaction [17,19], or the Ugi reaction [20]. The crystal structure of **5** has been published in 1976 [21]. The interest in the amino acid **5** is based on the biological activities of some of its derivatives, *e.g.*, as inhibitors of *S*-adenosyl L-methionine synthetase [19], glycogen phosphorylase inhibitor [22], or ecdysone agonist [23].

Heterocyclic amino acids of type **5** have also been used in the synthesis of conformationally restricted peptides [24]. Like other α,α-disubstituted α-amino acids, the presence of **5** forces peptides to form β-turns [12] or helical conformations. In our studies towards the synthesis of such sterically congested oligopeptides with a helical conformation by using the 'azirine/oxazolone method' [25–29], we introduced *N*-(2,2-dimethyl-2*H*-azirin-3-yl)proline methyl ester as a dipeptide (Aib-Pro) synthon [30–32] as well as other dipeptide (Xaa-Pro) synthons, including those with Xaa being a heterocyclic α-amino acid [13,33,34]. The aim of the present study was the synthesis of (*S*)-*N*-(1-aza-6-thiaspiro[2.5]oct-1-en-2-yl)proline methyl ester (**1c**) and its use as a (*S*)-*N*-[(4-aminotetrahydro-2*H*-thiopyran-2-yl)carbonyl]proline (Tht-Pro) synthon.

2. Results and discussion

2.1. *Synthesis of the Heterospirocyclic Azirine* **1c**. As the method of Villalgordo for the synthesis of 2*H*-azirin-3-amines **1** [35], used by Strässler for the preparation of **1b** (n = 1) [12], is limited to *N*-alkyl-*N*-phenyl derivatives, we decided to prepare *N*-[(tetrahydro-2*H*-thiopyran-4-yl)thiocarbonyl]-L-proline methyl ester (**9**), with the aim of following the protocol of the aminoazirine synthesis published by Rens and Ghosez [36] and modified by Dietliker [37]. Thus, tetrahydro-2*H*-thiopyran-4-carboxylic acid

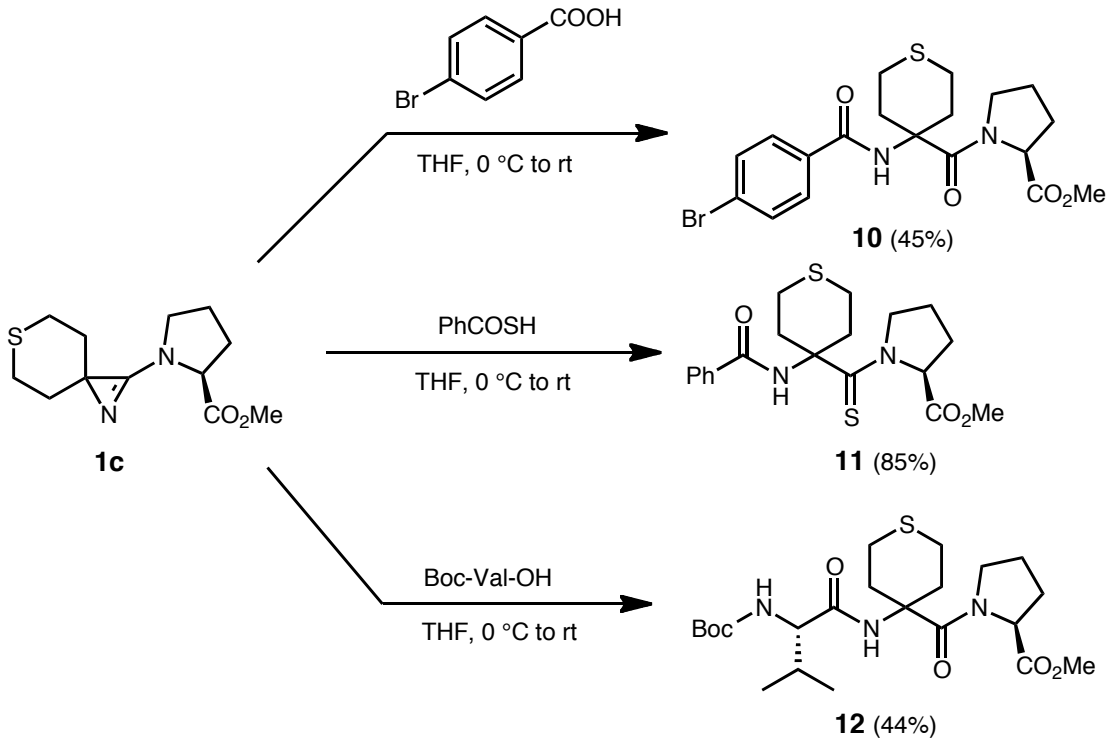
chloride (**6**) [12] was reacted with L-proline methyl ester (**7**) to give *N*-[(tetrahydro-2*H*-thiopyran-4-yl)carbonyl]-L-proline methyl ester (**8**) in 85% yield, which was converted to **9** by thionation with Lawesson reagent in 67% yield (Scheme 2). In analogy to the procedure described in [30] and to the protocol for the synthesis of **1b** (X = O, *n* = 1) [34], consecutive treatment of a solution of **9** in CH_2Cl_2 and catalytic amounts of DMF with $COCl_2$, evaporation of the solvent, dissolution of the residue in THF, addition of 1,4-diazabicyclo[2.2.2]octane (DABCO), filtration, and reaction with NaN_3 gave azirine **1c** in 67% yield. Because of the decomposition of the crude product during its purification using column chromatography (SiO_2), the compound was used in the next reactions without further purification.



Scheme 2. Synthesis of the dipeptide (Tht) synthon **1c**

2.2. *Reactions of* **1c** *with Carboxylic and Thiocarboxylic Acids*. For the chemical characterization of **1c**, reactions with thiobenzoic acid (PhCOSH) and 4-bromobenzoic acid (*p*-BrBz-OH) were performed in THF at 0 °C to room temperature [34] (for reactions of **1c** with H_2O and H_2S, see [38]). After chromatographic workup

of the mixture of the reaction with *p*-BrBz-OH, the *p*-bromobenzoyl-dipeptide methyl ester **10** was isolated in 45% yield. Similarly, after successful chromatography, the *N*-benzoylated endothiopeptide methyl ester **11** was obtained in 85% yield (Scheme 3).



Scheme 3. Reactions of **1c** with carboxylic, thiocarboxylic, and amino acids

With the aim of testing the utility of **1c** as a dipeptide synthon (Tht-Pro) in peptide synthesis, the reaction with Boc-protected L-valine (Boc-Val-OH) was carried out in THF. A solution of Boc-Val-OH (1 mol-equiv.) in THF was cooled to 0 °C. Then, **1c** (2 mol-equiv.) was added at 0 °C, and the mixture was stirred for 43 hours at room temperature. After chromatographic purification of the product, the *N*-protected tripeptide methyl ester Boc-Val-Tht-Pro-OMe (**12**) was obtained in 44% yield as a white foam (Scheme 3). Suitable single-crystals of **12** could be obtained from

$CHCl_3$/hexane by slow evaporation of the solvent, and its structure was established by an X-ray crystal-structure analysis (Figure 1).

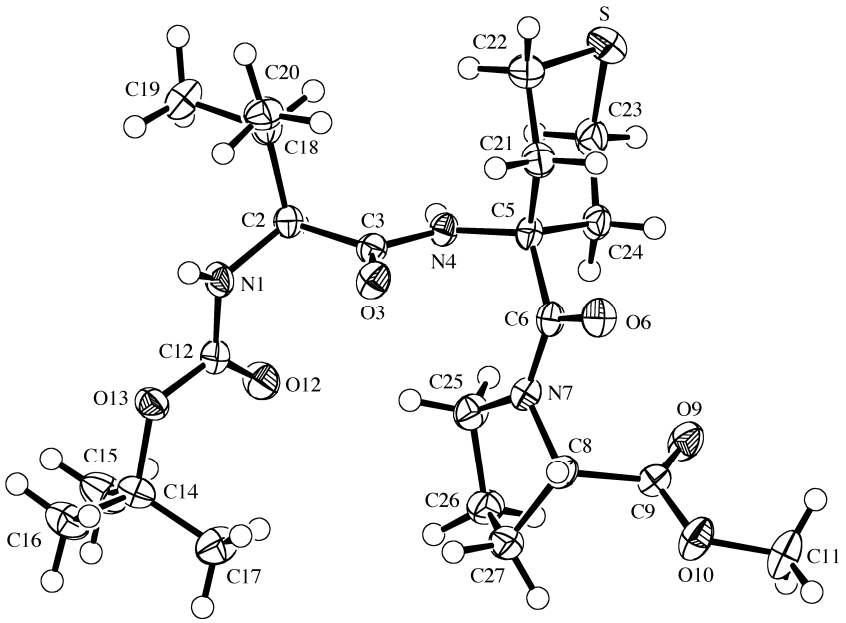


Figure 1. ORTEP plot [39] of the molecular structure of **12** (with 50% probability ellipsoids; arbitrary numbering of atoms)

Although there is no intramolecular H-bond present, the peptide backbone of **12** adopts a conformation resembling *β*-turns of Aib-containing oligopeptides. The torsion angles ϕ (C(6)-C(5)-N(4)-C(3)) and ψ (N(4)-C(5)-C(6)-N(7)) of the tetrahydro-2*H*-thiopyran-4-yl (Tht) residue are 53.1(2) and 38.9(2)°, respectively. They are close to the values expected for an amino acid in a *β*-turn of type I or III. Each N-H group of the molecule acts as a donor for intermolecular H-bonds: N(1)-H forms an intermolecular H-bond with the ester carbonyl O-atom at the opposite end of a neighboring molecule (N(1)···O(9'): 2.955(2) Å, angle 170(2)°). This interaction links the molecules into extended one-dimensional chains which run parallel to the

[010] direction and have a graph set motif [40] of C(11). N(4)-H interacts with the secondary amide O-atom of a different neighboring molecule (N(4)···O(6'')): 2.976(2) Å, angle 167(2)°), and thereby links the molecules into extended one-dimensional chains which run parallel to the [100] direction and have a graph set motif of C(5). The combination of both interactions links the molecules into a two-dimensional network, which lies parallel to the (001) plane (Figure 2).

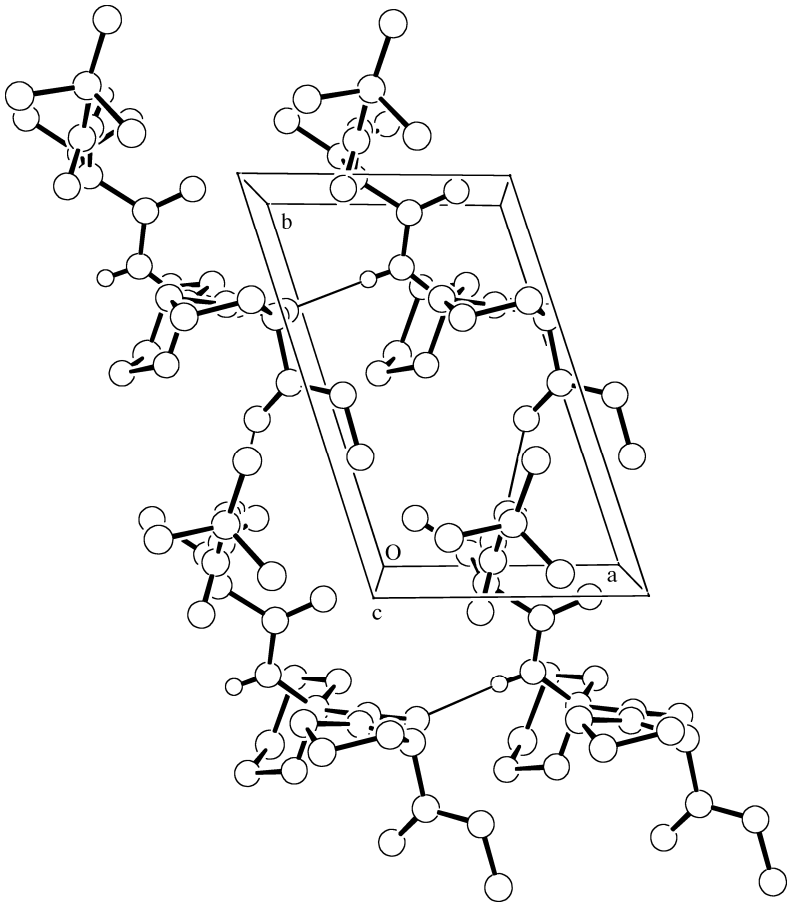


Figure 2. Crystal packing diagram of **12**, showing the H-bonding interactions (uninvolved H-atoms omitted for clarity).

3. Conclusions

The studies presented show that the new spirocyclic *N*-(2*H*-azirin-3-yl)proline derivative **1c** can be prepared according to previously reported protocols. In the reactions with PhCOSH, *p*-BrBz-OH, and *N*-protected α-amino acids, **1c** behaves like other 2*H*-azirin-3-amines (= 3-amino-2*H*-azirines) that have been used extensively as building blocks for α,α-disubstituted glycines in peptide synthesis. The novel amino azirine **1c** was shown to be a synthon for the dipeptide *N*-[(4-aminotetrahydro-2*H*-thiopyran-4- yl)carbonyl]-L-proline (Tht-Pro). In the crystal, the prepared tripeptide Boc-Val-Tht-Pro-OMe (**12**) adopts a β-turn conformation, despite the lack of the typical intramolecuar hydrogen bond. This is a further proof of the intrinsic property of α,α-disubstituted α-amino acids to stabilize β-turns or 3_{10}-helical structures in peptides (see [32] and refs. cited therein).

4. Experimental

4.1. *General*

All purchased chemicals were of analytical grade and used without further purification; solvents were purified by standard procedures. TLC was performed using pre-coated aluminium sheets (Merck silica gel $60F_{254}$), and column chromatography (CC) on silica gel C-560 (230–400 mesh; Uetikon-Chemie). Melting points were determined on a Büchi Melting Point B-450 apparatus and are not corrected. IR spectra were recorded on a Perkin-Elmer, Spectrum one FT-IR spectrophotometer in KBr (cm^{-1}), ^{1}H (300 or 600 MHz) and ^{13}C NMR spectra (75.6 or 150 MHz) on a Bruker AC-300 or Bruker DRX-600 spectrometer in $CDCl_3$ (ppm, J in Hz), ^{13}C-signal multiplicity from DEPT spectra, and mass spectra on a Finnigan SSQ-

700 (CI with NH_3) or Finnigan TSQ-700 (ESI) instrument, significant peaks in m/z (rel. %).

4.2. ***Synthesis of (S)-N-[(tetrahydro-2H-thiopyran-4-yl)carbonyl]proline methyl ester*** **(8)**.

To cooled MeOH (8 ml) was slowly added $SOCl_2$ (1.73 ml) keeping the temp. below 0 °C. Then, (*S*)-proline (2.53 g, 21.97 mmol) was added, and the mixture was heated at reflux for 1 h. Excess MeOH was evaporated, the sticky pale yellow crude methyl (*S*)-prolinate (**7**) was dissolved in AcOEt (8 ml), Et_3N (6.12 ml) and tetrahydro-2*H*-thiopyran-4-carbonyl chloride (**6**, 3.62 g, 21.97 mmol) [12] were added at 0 °C, and the mixture was stirred at rt overnight. After evaporation of AcOEt, the residue was dissolved in CH_2Cl_2, the solution was washed with sat. aqueous NaCl solution, dried over $MgSO_4$, CH_2Cl_2 was evaporated, and the residue was distilled (bulb-to-bulb, 190 °C/5.10–2 mbar): 4.81 g (85%) of **8**. Pale yellow oil. IR (film): 2951*s*, 1744*s*, 1643*s*, 1434*s*, 1357*m*, 1303*w*, 1271*m*, 1239*w*, 1197*s*, 1175*s*, 1116*w*, 1096*w*, 1029*w*, 1012*w*, 934*m*, 733*m*. ^{1}H-NMR: 4.49–4.45 (*m*, CH(α)(Pro)); 3.72 (*s*, MeO); 3.68–3.65, 3.58–3.53 (2*m*, CH_2(δ)(Pro)); 2.73–2.71 (*m*, CH_2(2), CH_2(6)(Tht)); 2.46–2.42 (*m*, CH(4)(Tht)); 2.20–2.06 (*m*, 3 H); 2.02–1.89 (*m*, 5 H). ^{13}C-NMR: 173.5, 172.7 (2*s*, 2 C=O); 58.5 (*d*, CH(α)(Pro)); 52.0 (*q*, MeO); 46.7 (*t*, CH_2(δ)(Pro)); 42.5 (*d*, C(4)(Tht)); 30.1, 29.8 (2*t*, C(2), C(6)(Tht)); 29.5 (*t*, CH_2(β)(Pro)); 27.7, 27.6 (2*t*, C(3), C(5)(Tht)); 24.7 (*t*, CH_2(γ)(Pro)). CI-MS: 275 (30, $[M + NH_4]^+$), 258 (100, $[M + H]^+$).

4.3. ***Synthesis of (S)-N-[(tetrahydro-2H-thiopyran-4-yl)thiocarbonyl]-proline methyl ester*** **(9)**.

To a solution of **8** (3.89 g, 15.1 mmol) in abs. toluene (46 ml) was added Lawesson

reagent (7.4 g, 18.3 mmol), and the mixture was stirred at reflux for 4 h and then at r.t. overnight. Then, the mixture was filtered (Celite), the solvent evaporated and the crude product was purified by gradient chromatography (SiO_2, CH_2Cl_2/MeOH from 200:1 to 150:1) to give 2.77 g (67%) of **9**. Pale yellow oil. ^{1}H-NMR: 5.15 (*dd*, *J* = 8.6, 8.4 CH(α)(Pro)); 3.91–3.85, 3.77–3.75 (2*m*, CH_2(δ)(Pro)); 3.72 (*s*, MeO); 2.84–2.63 (*m*, 5 H); 2.31–2.00 (*m*, 8 H). ^{13}C-NMR: 206.1 (*s*, C=S); 170.9 (*s*, C=O); 64.9 (*d*, CH(α)(Pro)); 52.2 (*q*, MeO); 50.2 (*t*, CH_2(δ)(Pro)); 49.0 (*d*, C(4)(Tht)); 33.4, 32.9 (2*t*, C(2), C(6)(Tht)); 28.6, 28.2 (2*t*, C(3), C(5)(Tht)); 28.0 (*t*, CH_2(β)(Pro)); 24.5 (*t*, CH_2(γ)(Pro)). EI-MS: 273 (100, M^+), 226 (37), 212 (43).

4.4. ***Synthesis of methyl (S)-N-(1-aza-6-thiaspiro[2.5]oct-1-en-2-yl)proline methyl ester*** **(1c)**. In a dried two-neck round-bottom flask, a solution of **9** (2.5 g, 9.14 mmol) in abs. CH_2Cl_2 (11 ml) and 3 drops of DMF was cooled to 0 °C. After slow addition of 5.5 ml of a $COCl_2$ solution in toluene (2M, 11 mmol), the mixture was stirred at rt for 1 h, and then the solvent was evaporated. The residue was dissolved in THF (22.5 ml), DABCO (1.23 g, 11 mmol) was added at 0 °C, and the mixture was stirred at rt for 40 min. The solid was removed by filtration under Ar and washed with THF. To the pale yellow solution was added NaN_3 (1.78 g, 27.42 mmol), the mixture was stirred at rt overnight, filtered through a Celite pad, and the solvent was evaporated. The residue was dissolved in AcOEt, the solution was washed with sat. aqueous $NaHCO_3$ and NaCl solution, the organic layer was dried over $MgSO_4$, and evaporated. The crude product **1c** was obtained in 67% yield. It could not be purified by chromatography because of decomposition, therefore, it was used without further purification.

4.5. ***General procedure for reactions of*** **1c** ***with PhCOSH,*** **p-*BrBz-OH, and Boc-Val-OH***.

To a solution of the acid in dry THF at 0 °C, a solution of ca. 2 mol-equiv. of **1c** in dry THF was added dropwise. The mixture was stirred at rt. After completion of the reaction (TLC), the solvent was evaporated in vacuo and the residue was purified by gradient CC (SiO_2; CH_2Cl_2/MeOH).

4.5.1. *(*S*)*-N-*({4-[(4-Bromobenzoyl)amino]tetrahydro-2*H*-thiopyran-4-yl}carbonyl)proline methyl ester* (*p*-BrBz-Tht-Pro-OMe, **10**).

According to the general procedure, *p*-BrBz-OH (196 mg, 0.975 mmol) and **1c** (496 mg, 1.950 mmol), stirring for 20 h, and CC (CH_2Cl_2/MeOH from 150:1 to 40:1) gave 199.8 mg (45%) of **10**. White foam. M.p. 238–239 °C. IR: 3331*m*, 2951*m*, 2924*m*, 1744*s*, 1651*s*, 1617*s*, 1591*m*, 1567*w*, 1530*s*, 1482*s*, 1440*m*, 1407*m*, 1359*m*, 1315*w*, 1298*w*, 1279*w*, 1245*w*, 1207*m*, 1174*s*, 1112*w*, 1066*m*, 1040*w*, 1011*m*, 760*m*. ^{1}H-NMR (CD_3OD): 7.78–7.74 (*m*, 2 arom. H); 7.69–7.64 (*m*, 2 arom. H); 4.51–4.48 (*m*, CH(α)(Pro)); 3.78–3.75 (*m*, 1 H); 3.72 (*s*, MeO); 2.97–2.83 (*m*, 2 H); 2.76–2.52 (*m*, 3 H); 2.41–2.18 (*m*, 3 H); 2.11–1.82 (*m*, 5 H). ^{13}C-NMR (CD_3OD): 173.3, 171.0 (2*s*, 2 C=O); 165.5 (*s*, Ar*C*=O); 132.3 (*s*, 1 arom. C); 131.8, 128.7 (2*d*, 4 arom. CH); 126.6 (*s*, 1 arom. C); 60.6 (*d*, CH(α)(Pro)); 58.6 (*s*, C(4)(Tht)); 52.0 (*q*, MeO); 47.6 (*t*, CH_2(δ)(Pro)); 33.3, 32.8, 27.4, 25.7, 24.2, 23.1 (6*t*, 6 CH_2). ESI-MS: 479 (100, [*M*(^{81}Br) + Na]$^+$), 477 (96, [*M*(^{79}Br) + Na]$^+$).

4.5.2. *(*S*)*-N-*{[4-(Benzoylamino)tetrahydro-2*H*-thiopyran-4-yl]thiocarbonyl}proline methyl ester* (Bz-Tht-*Ψ*(CS)-Pro-OMe, **11**). According to the general procedure, PhCOSH (28 mg, 0.203 mmol) and **1c** (103.4 mg, 0.407 mmol), stirring for 90 h, and

CC (CH_2Cl_2/MeOH from 150:1 to 110:1) gave 67.7 mg (85%) of **11**. White foam. M.p. 139–140 °C. IR: 3452*m*, 2949*m*, 2924*m*, 1741*s*, 1638*s*, 1601*w*, 1579*m*, 1449*w*, 1409*s*, 1348*w*, 1276*m*, 1248*m*, 1203*m*, 1171*s*, 1107*m*, 1057*w*, 1043*w*, 1001*m*, 965*m*, 877*m*, 799*m*, 716*s*, 646*m*. ^{1}H-NMR (CD_3OD): 7.59 (*d*, *J* = 7.0, 2 arom. H); 7.61–7.48 (*m*, 3 arom. H); 5.06 (broad *d*, *J* = 6.3, CH(α)(Pro)); 4.06–4.00 (*m*, 1 H); 3.68 (*s*, MeO); 3.59–3.53 (*m*, 1 H); 3.21–3.11 (*m*, 1 H); 2.91–2.80 (*m*, 3 H); 2.59–2.55 (*m*, 3 H); 2.25–1.90 (*m*, 5 H). ^{13}C-NMR (CD_3OD): 206.2 (*s*, C=S); 173.1 (*s*, C=O); 168.9 (*s*, Ph*C*=O); 135.3 (*s*, 1 arom. C); 133.1, 129.8, 127.8 (3*d*, 5 arom. CH); 70.2 (*d*, CH(α)(Pro)); 64.6 (*s*, C(4)(Tht)); 54.0 (*q*, MeO); 53.7 (*t*, CH_2(δ)(Pro); 36.8, 36.1, 28.5, 26.9, 24.9, 24.1 (6*t*, 6 CH_2). CI-MS: 410 (32, $[M + NH_4]^+$), 393 (100, $[M + H]^+$), 361 (78, $[M – OMe]^+$), 272 (17).

4.5.3. *(*S*)*-N-*{[4-({(2*S*)-2-[(*tert*-Butoxycarbonyl)amino]-3-methylbutanoyl}amino)-tetrahydro-2*H*-thiopyran-4-yl]carbonyl}proline methyl ester* (Boc-Val-Tht-Pro-OMe, **12**).

According to the general procedure, Boc-Val-OH (126.4 mg, 0.582 mmol) and **1c** (296 mg, 1.164 mmol), stirring for 43 h, and CC (CH_2Cl_2/MeOH from 150:1 to 110:1) gave 120 mg (44%) of **12**. White foam. M.p. 225–226 °C. IR: 3370*s*, 3321*s*, 2974*m*, 1732*s*, 1711*s*, 1686*s*, 1603*s*, 1528*s*, 1427*m*, 1391*w*, 1361*m*, 1322*w*, 1276*w*, 1245*m*, 1220*m*, 1171*s*, 1097*m*, 1068*w*, 1039*w*, 985*m*, 924*m*, 881*m*, 609*m*. ^{1}H-NMR: 7.24 (*s*, NH); 5.06 (*d*, *J* = 8.9, NH(Val)); 4.58–4.50 (*m*, CH(α)(Pro)); 3.86–3.83 (*m*, CH(α)(Val)); 3.71 (*s*, MeO); 3.64–3.62, 3.60–3.51 (2*m*, CH_2(δ)(Pro)); 3.10–2.87 (*m*, 1 H); 2.68–2.59 (*m*, 4 H); 2.20–2.16 (*m*, CH(β)(Val)); 2.12–1.98 (*m*, 5 H); 1.89–1.83 (*m*, 2 H); 1.46 (*s*, 9 H, Me_3C); 1.00–0.94 (2*d*, *J* = 6.8, 2 Me(Val)). ^{13}C-NMR: 173.0, 170.3, 170.0 (3*s*, 3 C=O); 155.9 (*s*, C=O(Boc)); 80.1 (*s*, Me_3C); 60.5 (*d*, CH(α)(Pro));

60.1 (*d*, CH(α)(Val)); 58.1 (*s*, C(4)(Tht)); 51.9 (*q*, MeO); 47.4 (*t*, CH_2(δ)(Pro)); 33.3, 33.2 (2*t*, C(2), C(6)(Tht)); 30.1 (*d*, CH(β)(Val)); 28.2 (*q*, Me_3C); 27.5 (*t*, CH_2(β)(Pro)); 25.9 (*t*, CH_2(γ)(Pro)); 24.2, 23.2 (2*t*, C(3), C(5)(Tht)); 19.5, 17.9 (2*q*, 2 Me(Val)). ESI-MS: 494 (100, $[M + Na]^+$).

Suitable crystals of **12** for the X-ray crystal-structure determination were grown from $CHCl_3$/hexane by slow evaporation of the solvent at rt.

5. X-ray crystal-structure determination of 12

All measurements were made on a Nonius KappaCCD area-detector diffractometer [41] using graphite-monochromated MoK_α radiation (λ 0.71073 Å) and an Oxford Cryosystems Cryostream 700 cooler. Data reduction was performed with HKL Denzo and Scalepack [42]. The intensities were corrected for Lorentz and polarization effects, and an absorption correction based on the multi-scan method [43] was applied. Equivalent reflections, other than Friedel pairs, were merged. Data collection and refinement parameters are given below [44], and views of the molecule and the crystal packing are shown in Figures 1 and 2. The structures were solved by direct methods using SIR92 [45], which revealed the positions of all non-H-atoms. The non-H-atoms were refined anisotropically. The amide H-atoms were placed in the positions indicated by a difference electron density map, and their positions were allowed to refine together with individual isotropic displacement parameters. All remaining H-atoms were placed in geometrically calculated positions and refined using a riding model where each H-atom was assigned a fixed isotropic displacement parameter with a value equal to 1.2U_{eq} of its parent C-atom (1.5U_{eq} for the methyl groups). Refinement of the structure was carried out on F^2 using full-matrix least-squares procedures, which minimized the function $\Sigma w(F_o^2\text{-}F_c^2)^2$. A correction for

secondary extinction was applied. Refinement of the absolute structure parameter [46] yielded a value of –0.01(5), which confidently confirms that the refined coordinates represent the true enantiomorph. Neutral atom scattering factors for non-H-atoms were taken from ref. [47], and the scattering factors for H-atoms were taken from ref. [48]. Anomalous dispersion effects were included in F_c [49]; the values for f' and f'' were those of ref. [50]. The values of the mass attenuation coefficients are those of ref. [51]. All calculations were performed using the SHELXL97 [52] program.

***Crystal data for* 12**: $C_{22}H_{37}N_3O_6S$, M = 471.61, crystallized from CH_3Cl/hexane, colorless, tablet, crystal dimensions 0.07 × 0.15 × 0.18 mm, triclinic, space group $P1$, Z = 1, reflections for cell determination 23944, 2θ range for cell determination 4 – 55°, a = 6.1889(2) Å, b = 10.0211(3) Å, c = 10.8337(4) Å, α = 95.567(1)°, β = 96.425(1)°, γ = 107.156(1)°, V = 631.96(4) Å^3, T = 160(1) K, D_X = 1.239 g·cm^{-3}, μ(MoK_α) = 0.168 mm^{-1}, scan type ϕ and ω, $2\theta_{(max)}$ = 55°, transmission factors (min; max) = 0.883; 0.990, total reflections measured 14952, symmetry independent reflections 5406, reflections with $I > 2\sigma(I)$ 4984, reflections used in refinement 5406, parameters refined 304, restraints 3; $R(F)$ [$I > 2\sigma(I)$ reflections] = 0.0335, $wR(F^2)$ [all data] = 0.0843 ($w = [\sigma^2(F_o^2) + (0.0367P)^2 + 0.0767P]^{-1}$, where $P = (F_o^2 + 2F_c^2)/3$), goodness of fit 1.052, secondary extinction coefficient 0.075(8), final Δ_{max}/σ 0.001, $\Delta\rho$ (max; min) = 0.23; –0.20 e Å^{-3}.

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Graphical Abstract